

Recently, a growing body of evidence from studies in urban areas throughout the world, including our recent studies in Southern California, has linked ambient air pollution to adverse birth outcomes including low birth weight (LBW), preterm birth, perinatal mortality, and cardiac birth defects. To address this research question further, we examined whether ambient air pollution levels during pregnancy influenced the risk of low birth weight (LBW) (<2,500g) or preterm (<37 weeks gestation) birth in infants born to women living in the South Coast Air Basin (SoCAB) of Southern California during 1994–2000. We focused specifically on ambient levels of CO and PM₁₀ (for which we observed effects previously) and, in addition, PM_{2.5} (for which measurement began in 1999–2000). In addition to evaluating a more recent time period during which air pollution levels in the SoCAB continued to decline, we addressed two specific methodologic issues related to our previous work: (1) differences in effect estimates when mapping women's home locations using residential addresses versus zip codes and thereby potentially reducing nondifferential exposure misclassification, and (2) the importance of PM_{2.5} versus PM₁₀ for these outcomes, since smaller particles penetrate deeper into the lung and can result in transfer of potentially toxic compounds into the bloodstream. We obtained residential addresses for each subject and geocoded home locations using a Geographic Information System (GIS) and used these locations to assign ambient air monitoring station concentrations as measures of exposure. We observed a 19% increase in risk of term LBW (OR=1.19, 95% CI=1.00–1.42) and a 13% increase in risk of preterm birth (OR=1.13, 95% CI=1.01–1.26) per one ppm increase in annual average CO when using this residential address mapping method. These results are similar to those observed in our previous studies that relied on zip codes to assign monitoring station concentrations and used 1989–1993 data. In addition, results will be presented for the impact of month- and trimester-specific exposures and the importance of ambient PM_{2.5} in comparison to PM₁₀ levels for these outcomes.

069 MOLECULAR EPIDEMIOLOGY STUDIES OF THE EFFECTS OF AIR POLLUTION.

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Possible impact of air pollution on biomarkers of exposure, effects and susceptibility was studied in two districts with different levels of air pollution. Organic compounds adsorbed to air particles (PM₁₀) induced DNA adducts and embryotoxicity *in vitro* and *in vivo* assays. The results indicate that carcinogenic polycyclic aromatic hydrocarbons (PAHs) are mostly responsible for the genotoxic activity, contributing to 45–50% of all DNA adducts induced by these complex mixtures. The placental bulky DNA adducts have been studied in relation to metabolic genotypes CYP1A1, EPHX, GSTM1 and NAT2, and plasma levels of cotinine, and vitamins A, C and E. DNA adduct levels were determined by ³²P-postlabeling assay. The data were analyzed by multiple regression analysis. The higher DNA adduct levels were observed in nonsmoking mothers delivering children with IUGR (intrauterine growth retardation), and were affected by smoking, genotypes, vitamin C level, and education status. The results of DNA adduct analysis in placentas are complementary with *in vitro* DNA binding activity and embryotoxicity studies. The effect of CYP1A1 and CYP19 gene expressions was also investigated. CYP1A1 activity was enhanced in placentas of mothers from polluted district, while CYP19 activity was suppressed. Our results indicate the effect of environmental endocrine disruptors, such as PAHs. The activities of both enzymes could modulate DNA adducts in placental tissues. Our results imply the use of biomarkers for the evaluation of the impact of air pollution on pregnancy outcome. PAHs are the important element of the genotoxic and embryotoxic activity of complex organic mixtures adsorbed on respirable particles. Supported by the Czech Ministry of Environment (grant VaV/340/2/00).

070 PRENATAL AND EARLY CHILDHOOD HEALTH EFFECTS OF AIR POLLUTION IN THE CZECH REPUBLIC

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Ambient air pollution appears to increase mortality in infants, but effects on morbidity have not been well-studied. We have initiated follow-up of a birth cohort from the Czech Republic representing deliveries in two districts during 1994–1999. One of the districts, Teplice, is known for its high air pollution from power plants and coal home heating. The other, Prácheň, is characterized by lower levels of air pollution. The focus of this research is on immune parameters measured at birth and childhood morbidity in the first 4 ½ years of life. We found that lymphocyte distributions in maternal and/or cord blood were different in the two districts, with lower percentages of CD3+ ("T") cells in Teplice and higher percentages of natural killer (NK) cells in the more polluted district. Quantitative measures of air pollutants were also examined within Teplice, in analyses that controlled for the weekly rate of infections. Higher PM₁₀ exposures during the last 30 days prior to birth were associated with a lower percentage of CD3+ cells in both maternal and cord blood; with a lower percentage of CD8+ cells in maternal blood; and with a higher percentage of CD19+ ("B") cells. Rates of childhood diagnoses of otitis media during the first three years of life were higher in Teplice than in Prácheň. Frequent occurrences of upper respiratory infections (more than four physician-diagnosed episodes) were also elevated in Teplice as compared with Prácheň. Finally, pneumonia, which was relatively rare, was slightly more common in children residing in Teplice. We are now collecting data at 4 ½ years of age on another three years of births. Response rates have been high. The final analyses will include about 1000 children for whom morbidity and growth will be available to three years or longer.

Farm Family Biomonitoring Studies of Selected Herbicides/Insecticides: Implications for Epidemiologic Research

072 BIOMONITORING OF HERBICIDE EXPOSURE IN A FARM POPULATION.

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Various metrics have been used in exposure assessments of herbicides for epidemiologic studies. The most commonly used metric is a self-reported dichotomous indicator during a particular time period relevant to the health condition under study. However, this indicator represents an opportunity for exposure and is only the first in a series of events that may lead towards actual internal dose to the target tissues. Biological measurements are needed to measure absorbed or active doses. Very little information is available on the extent of exposure misclassification that may be associated with self-reported indicators of use. The Pesticide Exposure Assessment Study was designed to measure the extent to which applicators and family members on Ontario farms are exposed to herbicides and to identify some of the major factors affecting their exposure. The herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) or [4-chloro-2-methylphenoxy] acetic acid (MCPA) were selected as sentinel pesticides because they are widely used on Ontario farms and are rapidly excreted unchanged in the urine with a half-life of 12 to 72 hours. Farmers who had used these herbicides in an earlier cohort study of reproductive age couples were contacted by telephone to determine if they were planning on using these herbicides during the coming growing season. During the days when these herbicides were used for the first time during the season, the applicator, spouse and child collected a spot urine sample before handling the herbicides, and then 2 subsequent 24-hour (Day 1 and Day 2) urine samples. The applicator and spouse also completed questionnaires detailing the pesticides used and handling practices. Approximately 120 families participated in the biomonitoring study. MCPA levels in applicators' urine ranged from non-detectable to 800 µg/L with a mean of 32.1 and 41.7 µg/L for Day 1 and Day 2 urine, respectively. 2,4-D concentrations were lower, with a maximum value of 514 µg/L, and mean values of 11.1 and 15.7 µg/L for Day 1 and Day 2, respectively. Depending on the day of sampling and the herbicide, 12 to 20% of the children's samples were positive for 2,4-D or MCPA. Similarly for the wives of the applicators, 5 to 18% of the urine samples were positive. For those applicators that reported use of 2,4-D, urine levels ranged from non-detectable to 514 µg/L; similarly MCPA levels in MCPA applicators' urine ranged from non-detectable to 800 µg/L. These results demonstrate the exposure measurement errors that can occur when a self-reported dichotomous indicator of exposure is used in epidemiologic studies. Further refinement of the self-reported exposure metric by incorporating variables such as use of protective clothing or equipment, smoking status, pesticide formulation, type of application equipment, handling practices, and personal hygiene practices will improve exposure characterization in epidemiologic studies where it is not feasible to collect individual biological samples. As the sample size was small and the number of potential predictive variables large, similar studies should be conducted to assess the reproducibility of these results.

073 USE OF BIOMONITORING AND QUESTIONNAIRE DATA IN ASSESSMENT OF PESTICIDE EXPOSURES FOR STUDIES OF CHRONIC DISEASES AMONG FARMERS AND THEIR FAMILIES

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It is difficult to develop accurate assessments of pesticide exposures among farmers and their families relevant for the epidemiologic study of chronic diseases. Exposures among farmers typically occur for only a few days at intermittent periods through the year. Exposures to dependents of farmers would typically have similar patterns and, in addition, may be quite low. If these conditions did not present enough difficulty, assessment is further complicated because the relevant exposures for chronic diseases are those that may have occurred years in the past. Because of this need to determine exposures occurring years ago, investigators typically rely largely upon information from interviews. Although there is no way to directly monitor exposures to non-persistent pesticides in years past, current measurements can be used to quantitatively evaluate determinants of current exposure with the goal to use these as a window to determinants of past exposures. The three studies discussed in this session provide important information on the linkage between monitoring and questionnaire data, which is essential for the development of quantitative exposure estimates. Projects like these provide us with badly needed information to anchor our exposure estimates in epidemiologic studies and to determine where our current techniques fit along the reliability/validity scale. It is important to remember, however, that the measurement of exposures today is not the goal. This is a technique to help us to improve estimation procedures for exposures in the time-window of interest, i.e., the past. Monitoring data from today is not necessarily the Agold standard, but rather it is an indicator that must be evaluated for relevance to exposures from earlier times, just as we must evaluate the reliability of information reported by interview. This requires careful consideration of differences between current handling procedures and those from the past that may affect exposure levels and relationships with various exposure determinants. These include application equipment, mixing procedures, protective equipment and clothing, personal habits, chemicals used, application techniques, and others. This list should not result in an abandonment of the effort, but reinforce our need for data that allows us to thoroughly evaluate the reliability and accuracy of our assessment techniques.

074 PREVALENCE OF DETECTION OF HERBICIDES IN A SAMPLE OF RURAL RESIDENTS DURING SPRING HERBICIDE APPLICATION

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